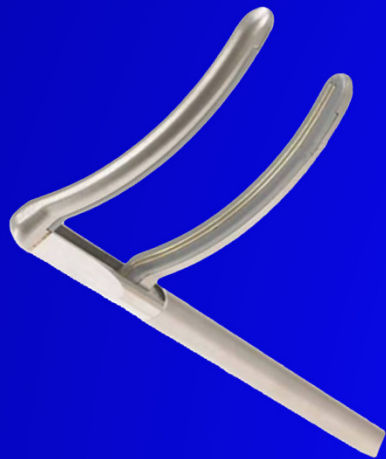


AtriCure Synergy Ablation System Circulatory System Devices Panel October 26, 2011



Clamp End Effector



Generator

Introduction

David J. Drachman

President & CEO, Director
AtriCure, Inc.

Proposed Refinement of the Current Indication

- Current indication
 - *“The AtriCure Synergy Ablation System is intended for the ablation of cardiac tissue during surgery.”*
- Proposed indication
 - *“The AtriCure Synergy Ablation System is intended to ablate cardiac tissue **for the treatment of persistent or long standing persistent atrial fibrillation in patients who are undergoing open concomitant coronary artery bypass grafting and/or valve replacement or repair.**”*

Prior Approvals and History

- U.S. clearance in 2001
- > 30 peer review publications
- > 500 U.S. centers used the Synergy system during 2010
- > 30 countries are using the system
- > 100,000 procedures performed with AtriCure bipolar clamps since 2002

Widespread Societal Support

- 2006 AF Guidelines
 - American College of Cardiology
 - American Heart Association
 - European Society of Cardiology
 - 2007 Heart Rhythm Society Consensus Statement
 - Heart Rhythm Society
 - European Heart Rhythm Association
 - European Cardiac Arrhythmia Society
 - Society of Thoracic Surgeons
- 2007 Society of Thoracic Surgeons - Surgical Ablation Guidelines

Approval of Indication Will Allow for an Extensive Training Program

- Proposed indication

*“The AtriCure Synergy Ablation System is intended to ablate cardiac tissue **for the treatment of persistent or long standing persistent atrial fibrillation in patients who are undergoing open concomitant coronary artery bypass grafting and/or valve replacement or repair.**”*

- Robust surgeon training program

- Post-approval study with 3-year follow-up

Training Program for $\approx 1,000$ Current Users and All New Users

- Training program
 - $\sim 1,000$ current users and all new users
 - 18 month timeline
 - Demonstrate knowledge and proficiency of Synergy system and Maze IV procedure
- Education Steering Committee – guide training

Presentation Agenda

EP Perspective	Hugh Calkins, MD <i>Professor of Medicine Director of Electrophysiology The Johns Hopkins Medical Institutions</i>
Surgical Perspective	Patrick McCarthy, MD, FACC <i>Chief, Division of Cardiac Surgery Northwestern Director, Bluhm Cardiovascular Institute</i>
AtriCure Sponsored Clinical Trials	James Edgerton, MD, FACC <i>Surgical Director, Heart Rhythm Center for Innovation Heart Hospital, Baylor Plano</i>
Training	David Drachman <i>President & CEO, Director AtriCure Inc.</i>
Post Approval Study	Lauren S. Baker, PhD <i>Boston Biomedical Associates</i>
Closing Remarks	Patrick McCarthy, MD, FACC

Invited Experts

**Thomas
Vander Salm, MD**

Clinical Professor, Harvard Medical School
Chief of Cardiac Surgery, North Shore
Medical Center

**Don Berry, PhD
Jason Connor, PhD**

Statistical Scientists,
Berry Consultants

Sydney Gaynor, MD

Medical Director of Clinical Education
AtriCure, Inc.

**Vigneshwar
Kasirajan, MD**

Professor of Surgery
Chairman, Division of Cardiothoracic Surgery
Virginia Commonwealth University

**Marc Gerdisch, MD
FACS, FACC**

Director of Cardiothoracic Surgery
St. Francis Heart Center in Indianapolis

Overview of Atrial Fibrillation

Hugh Calkins, MD

Professor of Medicine

Director of Electrophysiology

The Johns Hopkins Medical Institutions

Epidemiology of AF

- Most common sustained cardiac arrhythmia¹
- Affects more than 5 million Americans²
- Estimated 2050 prevalence of ~12 million
- Preferentially affects men and the elderly^{1,2}
- Lifetime risk of developing AF: ~1 in 4 for adults ≥ 40 years of age³

1. Lloyd-Jones D, et al. [published online ahead of print December 17, 2009]. *Circulation*. doi:10.1161/CIRCULATIONAHA.109.192667.

2. Miyasaka Y, et al. *Circulation*. 2006;114(2):119-125.

3. Lloyd-Jones DM, et al. *Circulation*. 2004;110(9):1042-1046.

AF Is Associated with Increased Thromboembolic Risk

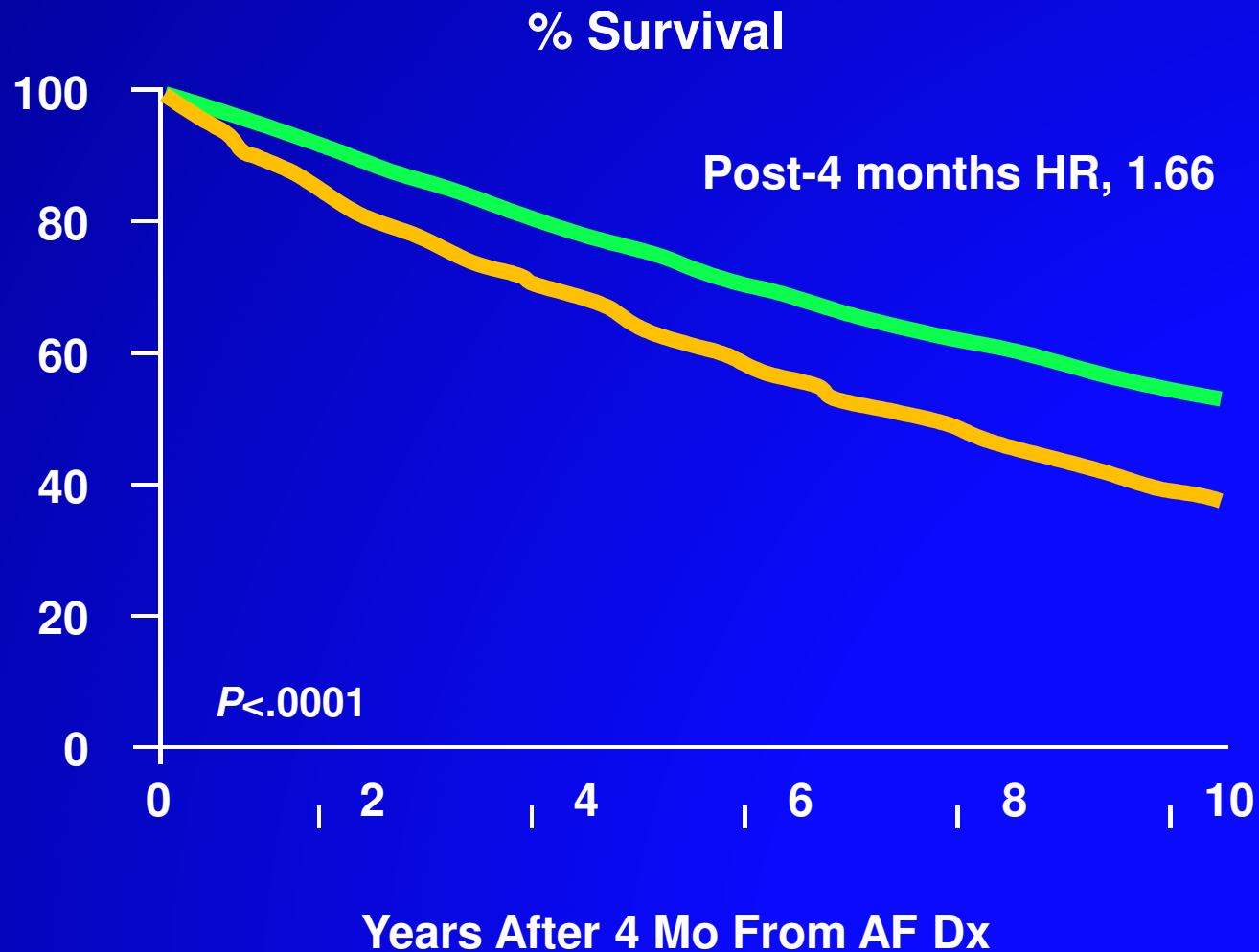
- Major cause of stroke in elderly¹
- 5-fold increase in risk of stroke^{1,2}
- 15% of strokes in US are attributable to AF³

1. Fuster V, et al. *J Am Coll Cardiol*. 2001;38(4):1231-1266.

2. Benjamin EJ, et al. *Circulation*. 1998;98(10):946-952.

3. Atrial Fibrillation Investigators. *Arch Intern Med*. 1994;154(13):1449-1457.

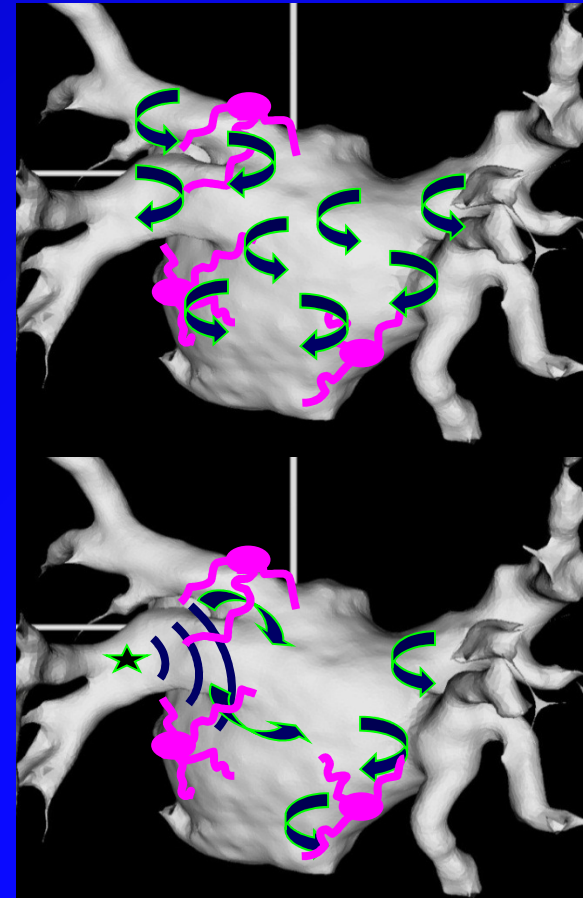
Mortality After Diagnosis of AF



Reproduced with permission from Miyasaka Y, et al. *J Am Coll Cardiol.* 2007;49(9):986-992.

Pathogenesis of AF

- Multiple-wavelet reentry¹
- Focal PV firing²



1. Moe GK, Abildskov JA. *Am Heart J.* 1959;58(1):59-70.
2. Konings KT, et al. *Circulation.* 1994;89(4):1665-1680.

AF is a Progressive Condition

- AF generally presents as intermittent AF
- Many patients progress to a continuous form over time
- Continuous AF results in electrical and structural remodeling of the atria
- The longer AF persists, the more difficult it is to restore and maintain sinus rhythm
- MAZE 4 procedure designed to treat persistent forms of AF

AF Classification in Clinical Guidelines

AF Classification	2006 AHA Guideline	2007 HRS Consensus Document
Paroxysmal	Recurrent AF (>2 episodes) Terminates spontaneously	
Persistent	Sustained episode > 7 days, or lasting < 7 days, but necessitating cardioversion	
Longstanding Persistent	Not defined	Continuous episode of > 1 year duration
Permanent	AF in which cardioversion has failed or has not been attempted	AF at a point in which no further rhythm control treatment is considered

Reconciliation of AF Classification for ABLATE

2006 AHA Guideline

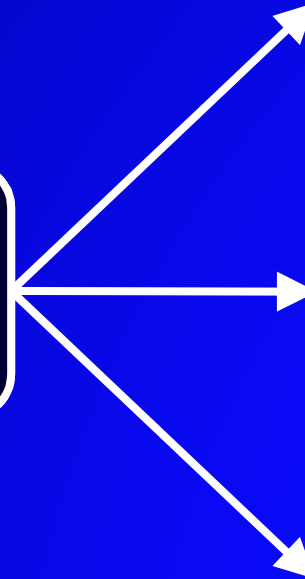
2007 HRS
Consensus Document

**ABLATE Patients:
Permanent
N=55**

**Paroxysmal
n=4**

**Persistent
n=22**

**Longstanding
Persistent
n=29**



FDA Commentary – Page 14

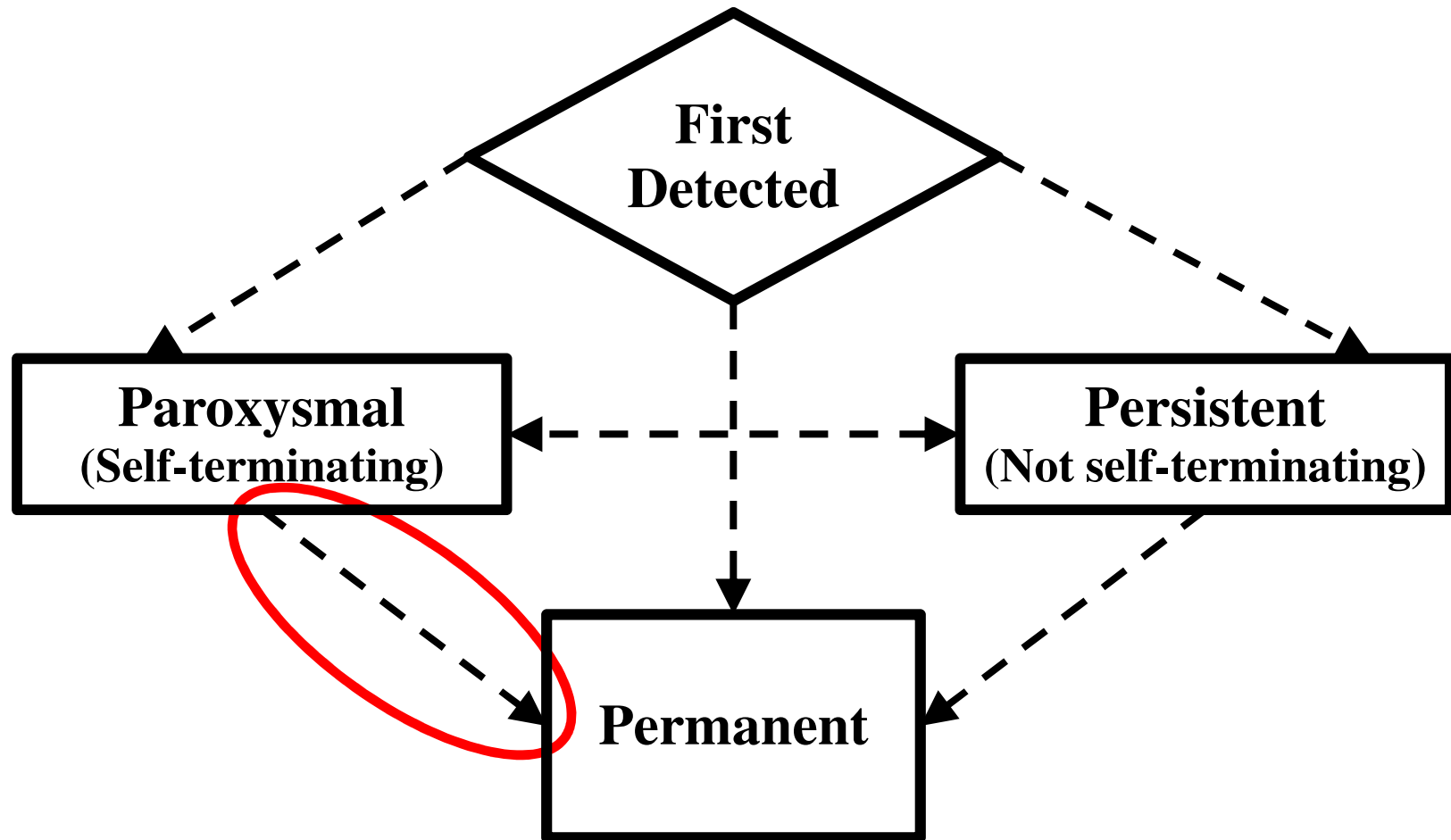
ABLATE was originally designed to assess the safety and effectiveness of the AtriCure Synergy Bipolar Ablation System in the treatment of subjects with *permanent* AF as defined in 2006, a term which was essentially abandoned in 2007. FDA notes the following:

1. FDA now typically associates the previous “permanent” designation with the contemporary AF classification “longstanding persistent.”
2. In their original submission, the Sponsor argued that patients with a long history of AF and associated comorbidities (e.g., enlarged left atria) could be considered “permanent”, even if the AF were self-terminating, paroxysmal AF. **FDA does not agree with this argument and believes that “permanent” (per 2006 Guidelines) implies continuous, non-self-terminating AF of duration at least one year, or that has failed cardioversion.**

AHA 2006 Guidelines for the Management of Patients with AF

- *“The category of persistent AF also includes cases of longstanding AF, usually leading to permanent AF, in which cardioversion has failed or not been attempted.”*
- *“The definition of permanent AF is often arbitrary. The duration of AF refers both to individual episodes and to how long the patient has been affected by the arrhythmia. Thus, a patient with paroxysmal AF may have episodes that last seconds to hours occurring repeatedly for years.”*

Figure 3. Patterns of atrial fibrillation (AF). 1, Episodes that generally last 7 d or less (most less than 24 h); 2, episodes that usually last longer than 7 d; 3, cardioversion failed or not attempted; and 4, both paroxysmal and persistent AF may be recur...



Fuster V et al. Circulation 2006;114:e257-e354

Patient Selection for Catheter Ablation of AF

Variable	More Optimal Catheter Patient	Less Optimal Catheter Patient
Symptoms	Highly symptomatic	Minimally symptomatic
Class I and III drugs failed	≥ 1	0
AF type	Paroxysmal	Persistent/ Longstanding Persistent
Age	Younger (<70 years)	Older (≥ 70 years)
LA size	Smaller (<5.0 cm)	Larger (≥ 5.0 cm)
Ejection fraction	Normal	Reduced
Congestive heart failure Other cardiac disease Pulmonary disease Sleep apnea Obesity Prior stroke/TIA	No	Yes

HRS 2007 Consensus Document: Indications for Surgical Ablation

- Symptomatic AF patients undergoing other cardiac surgery
- Selected asymptomatic AF patients undergoing cardiac surgery in whom the ablation can be performed with minimal risk

Final Thoughts

1. Patients enrolled in the ABLATE clinical trial would not have been appropriate candidates for catheter ablation
2. The EP Community generally believes that if a patient is undergoing cardiac surgery it is advised that their AF be addressed using a surgical approach while the chest is open

Atrial Fibrillation and Cardiac Surgery

Patrick M McCarthy, MD

Chief of the Division of Cardiac Surgery
Director Bluhm Cardiovascular Institute
Heller-Sacks Professor of Surgery in the
Feinberg School of Medicine

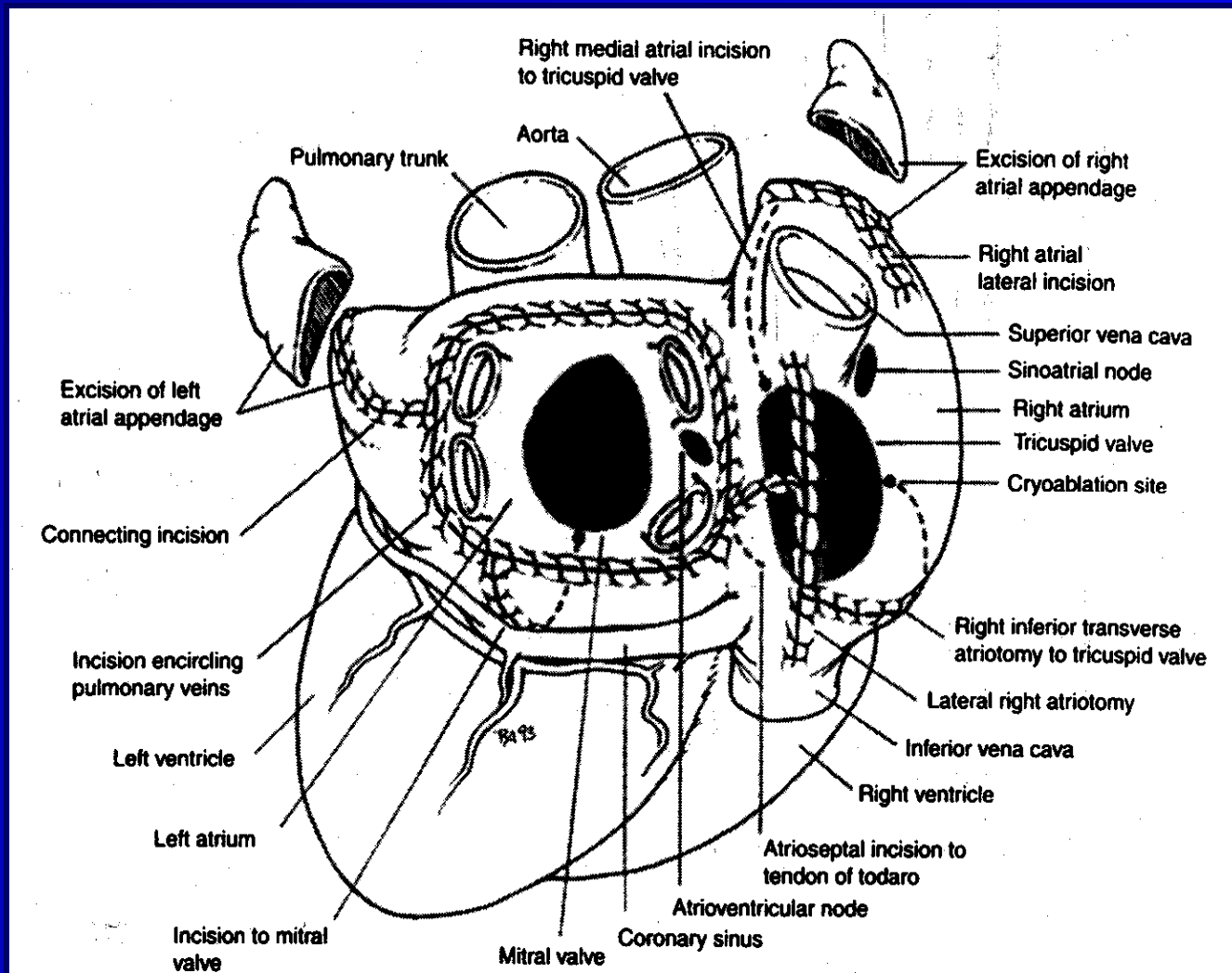


**Northwestern Memorial[®]
Hospital**

Overview

- Preoperative AF is common and contributes to morbidity and mortality
- RCTs and STS database indicate concomitant AF ablation is safe and effective
- Cardiac surgery and cardiology societies recommend concomitant AF ablation

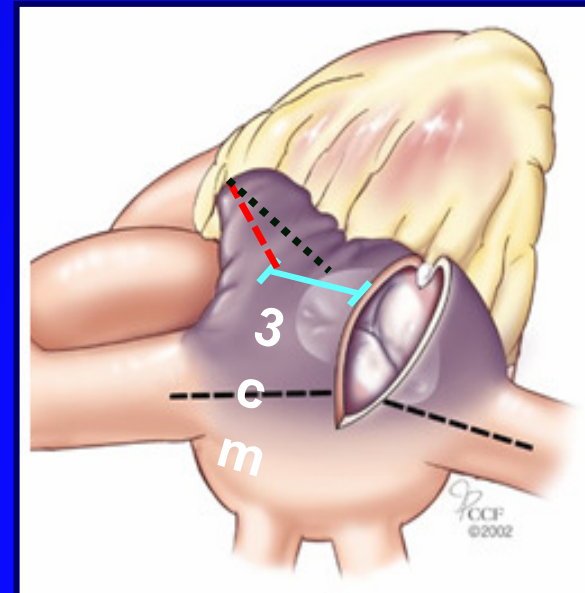
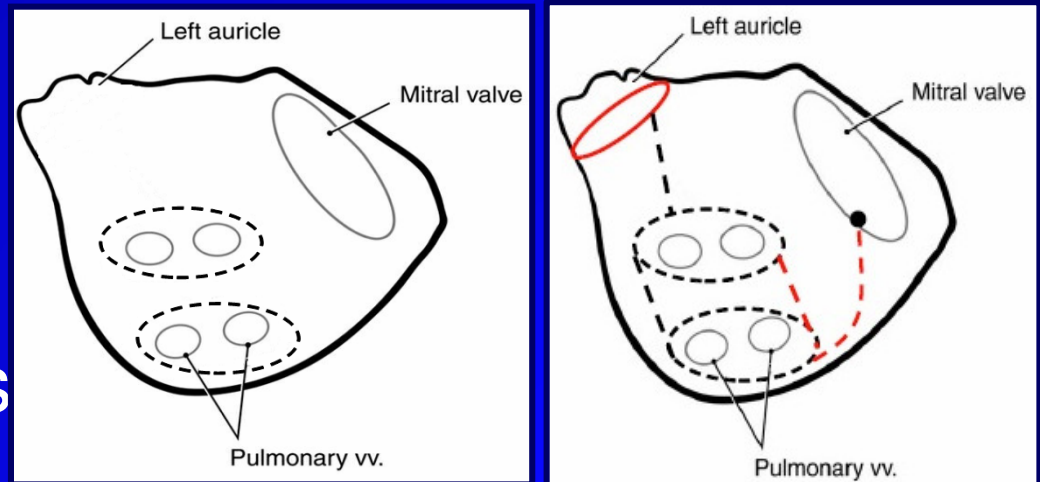
Cox-Maze Procedure



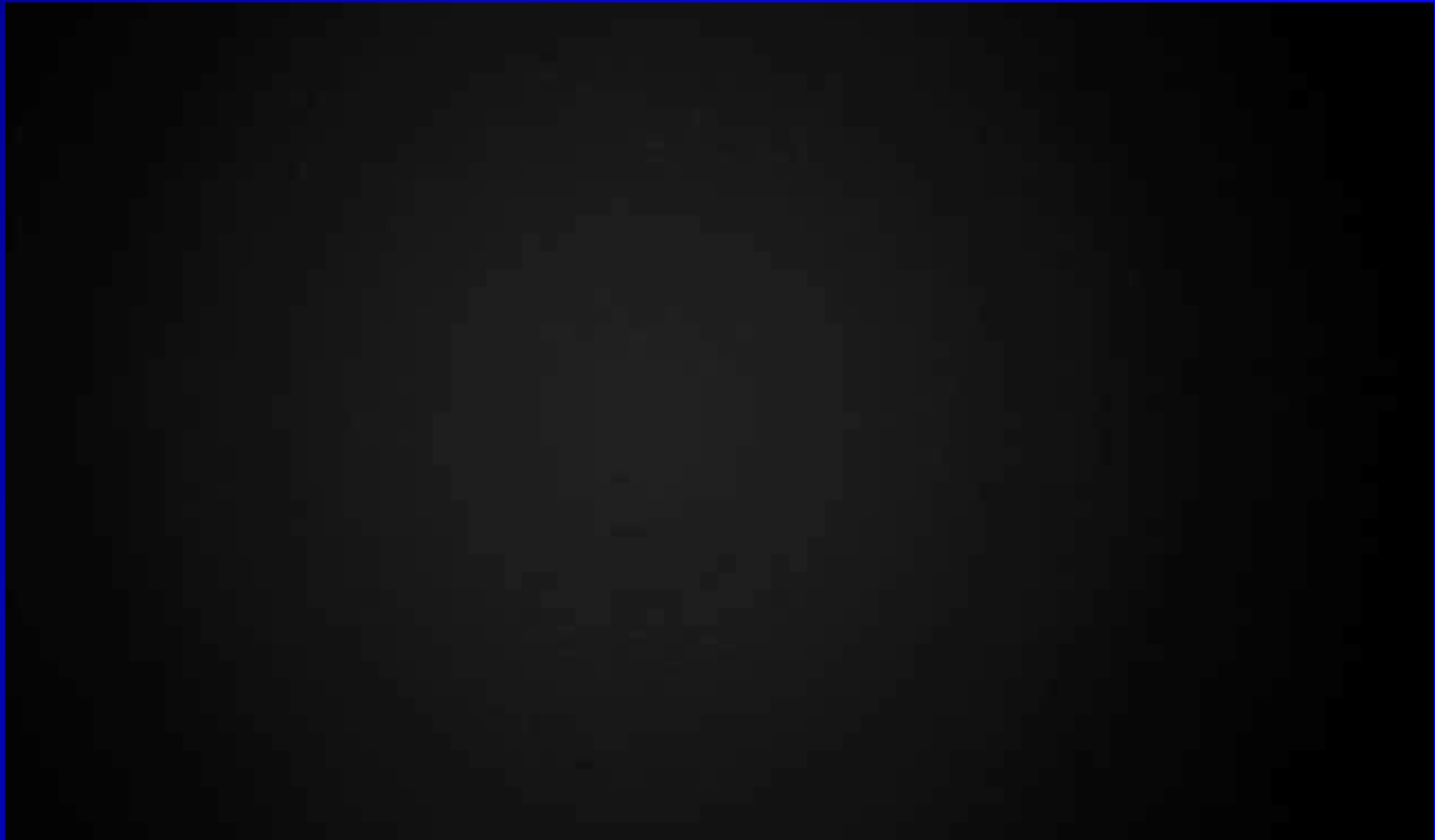
Reprinted with permission from Sundt TM 3rd, et al. *Cardiol Clin.* 1997;15(4):739-748.

Evolution of MAZE IV

- PV Isolation
- Left Atrial Lesions
- Right Atrial Lesions
- LA Appendage Removal/Exclusion



Maze IV Procedure Animation



Risks of Untreated AF: Mayo Clinic, Cleveland Clinic Investigations

- Compared subjects with Preoperative AF vs. no AF
- No AF Ablation surgery performed
- Statistical matching

Indication	Citation	Number of Patients
CABG	Quader et al Annals of Thor Surgery, 2004	46,984
Aortic Valve	Ngaage et al Annals of Thor Surgery, 2006	1,487
Mitral Valve	Ngaage et al Annals of Thor Surgery, 2007	2,821

Risks of Untreated AF: Cardiac Surgery Patients

CABG

- > 20% increase in mortality by 10 yrs
- Increased post op morbidity (2 X stroke)

Aortic Valve

- Worse late survival (RR = 1.5)
- More post op stroke (25% vs 10%) and CHF (16% vs 5%)

Mitral Valve

- 18% difference in survival by 10 yrs
- Increase in late cardiac events/stroke (32% difference)

Randomized Controlled Trials Support Concomitant AF Ablation

Primary Outcomes of Randomized Control Trials: Return of Normal Sinus Rhythm

Author, Year	Control 12 Month NSR	Treated 12 Month NSR	Method of Assessment
Deneke, 2002	26.7%	80% ($p = 0.005$)	Holter
Abreu Filho, 2005	26.9%	79.4% ($p = 0.001$)	24 hr ECG
Doukas, 2005	4.5%	44.4% ($p < 0.001$)	ECG (Holter if sx)
Chevalier, 2009	4%	57% ($p = 0.004$)	Holter
von Oppell, 2009	39%	75% ($p = 0.03$)	Holter

Randomized Control Trials: Secondary Outcomes

Outcome Parameter	Control	Treated	p-value
Max Work Stress Test ¹	43 ± 16	73 ± 29	p = 0.008
Shuttle Walk Distance ²	304 ± 120	359 ± 140	p = 0.02
LV ejection fraction %	54 ± 7	59 ± 7	p = 0.004
LVEDD (cm) ¹			
– 6 mo	4.33 ± 0.7	3.96 ± 0.7	p = 0.02
– 12 mo	4.26 ± 0.6	3.93 ± 0.7	p = 0.03
BNP (change from baseline to 12 mo)	30 ± 71	76 ± 125	p = 0.02

¹Deneke, 2002

²Doukas, 2005

STS Database Report: Safety Outcomes

- MV/AF ablation (n = 6,231) vs. No AF ablation (n = 5,214)
- Median XC and CPB 9-minute longer in AF ablation group

Outcome	Adjusted Odds Ratio	Adjusted p-value
Death	1.00	0.98
Any reoperation	0.98	0.80
Renal failure / dialysis	1.03	0.69
Prolonged ventilation	0.98	0.72
Post procedure LOS ≥ 14 days	1.00	0.95
Need for permanent pacemaker	1.26	0.007

Lessons from the STS Database

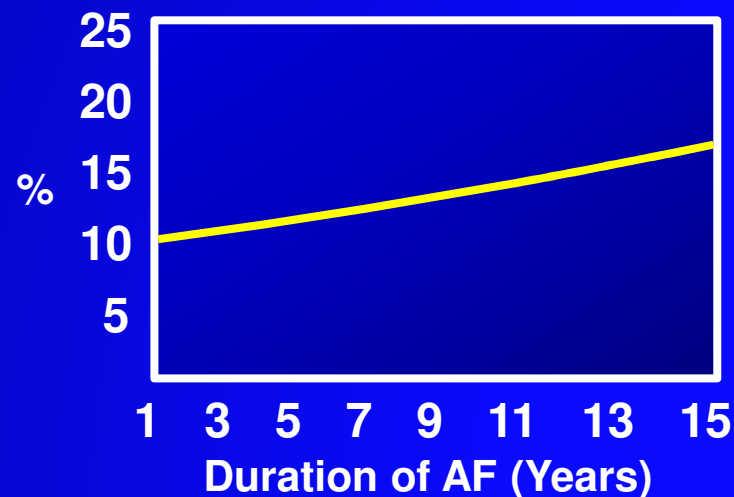
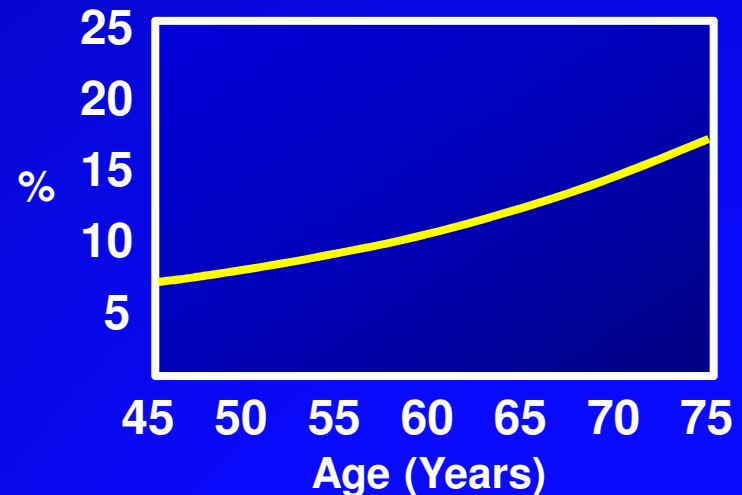
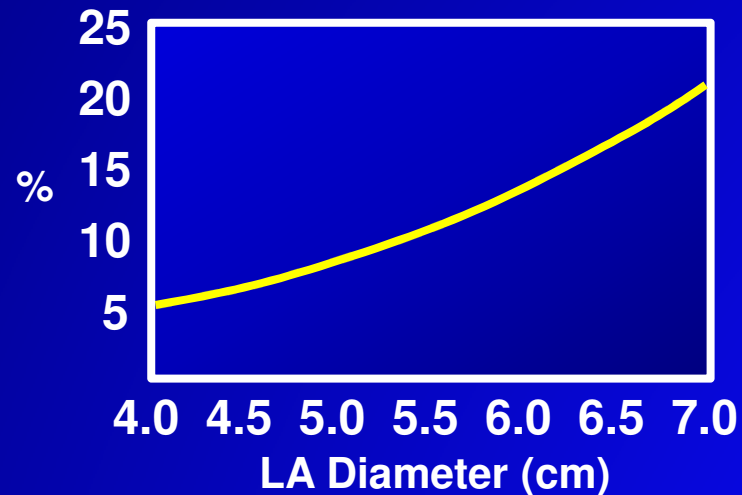
- *“After adjusting for differences in preoperative characteristics, mitral valve surgery patients with a surgical AF correction procedure did not have a significantly higher risk of mortality (adjusted OR: 1.00 [0.83, 1.20]) or major morbidity”*

Surgical AF Ablation Meta-analysis and Systematic Review

- 33 studies: 4,647 patients
- Discharge NSR: 68.6% vs. 23.0% (OR 7.15)
- 1-5 years; 74.6% vs. 18.4% (OR 6.7)
- No difference 30 day mortality

Patient Selection is Key

Predictors of AF Ablation Failure: 5 Yrs



Adapted from Gillinov et al., JTCVS, 2005; 130: 1653-1660

Consensus Statement, 2007

HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Personnel, Policy, Procedures and Follow-Up

A report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation.

“It is advisable that all patients with documented AF referred for other cardiac surgeries undergo a left or biatrial procedure for AF at an experienced center, unless it...will add significant risk...”

Summary

1. Untreated AF leads to impaired patient outcomes
2. RCT universally demonstrate higher normal sinus rhythm if AF is ablated
3. Safety in RCT; STS database; large single center studies is favorable
4. Therefore medical societies support concomitant AF ablation

Need for Accurate Labeling and Training

- Better training is needed
 - Efficacy is linked to technique
 - Safety needs to be reinforced
 - Patient Selection also determines success
 - Patient and referring physicians benefit from ready access to information

Clinical Data

AtriCure Synergy Ablation System

James Edgerton, MD

Surgical Director of the
Heart Rhythm Center for Innovation
Heart Hospital

ABLATE Clinical Trial Design

- Prospective, multi-center, single-armed
- Bayesian adaptive statistical design
 - Demonstrate non-inferiority to Objective Performance Criteria
 - Interim enrollment decision points
- Sample Size: 50 – 100 patients
- Procedure:
 - Lesion set is the standard Maze IV¹
 - Concomitant to open procedures

Key Inclusion Criteria

- ≥ 18 years of age
- History of *permanent AF* in which cardioversion (electrical and/or pharmacologic) has failed or has not been attempted*
- Scheduled to undergo elective cardiac surgical procedure(s) to be performed on cardiopulmonary bypass
- Left Ventricular Ejection Fraction $\geq 30\%$

* As defined by the 2006 ACC/AHA/ESC Guidelines.

Key Exclusion Criteria

- Class IV NYHA heart failure symptoms
- Preoperative need for intra-aortic balloon pump or intravenous inotropes
- LA size greater than or equal to 8 cm
- CVA within prior 6 months
- MI within the 6 weeks
- Need for emergent cardiac surgery
- Renal failure requiring dialysis or hepatic failure

ABLATE Primary Endpoints

- Primary Safety Endpoint
 - Composite of Death, Stroke, TIA, MI and Excessive Bleeding within 30 days or prior to hospital discharge
- Primary Efficacy Endpoint
 - AF Free (24-hr Holter) and off Class I and III antiarrhythmic drugs at 6 months
 - AF-free is defined as
 - No atrial fibrillation episodes > 5 minute in duration
 - ≤ 1 hour total atrial fibrillation in 24-hours

Additional Safety Endpoints

- Composite 6 month primary adverse event rate
- Overall adverse event rate at 6 months
- Pacemaker implantation rate

Additional Efficacy

- Proportion of patients AF free and:
 - Independent of AADs at 6 months (24-hour Holter)
 - Off AADs at 12 months (48-hour Holter)
 - Independent of AADs at 12 months (48-hour Holter)
- Reduction of AF burden on 48-hour Holter at 12 months
- Reduction of AF burden on 24-hour Holter at 6 months
- PV isolation effectiveness based on conduction block

Study Safety Success Criteria

- Performance Goal = 13.95% rate for acute major adverse events
- 5% margin
- Upper bound 18.95%
- **Success:** 95% posterior probability that the Composite Safety Endpoint $< 18.95\%$

Study Efficacy Success Criteria

- Performance Goal = 70% AF free and off anti-arrhythmic drugs at 6 months
- 10% margin
- Lower bound 60%
- **Success:** 97.5% posterior probability that the 6-month efficacy rate $> 60\%$

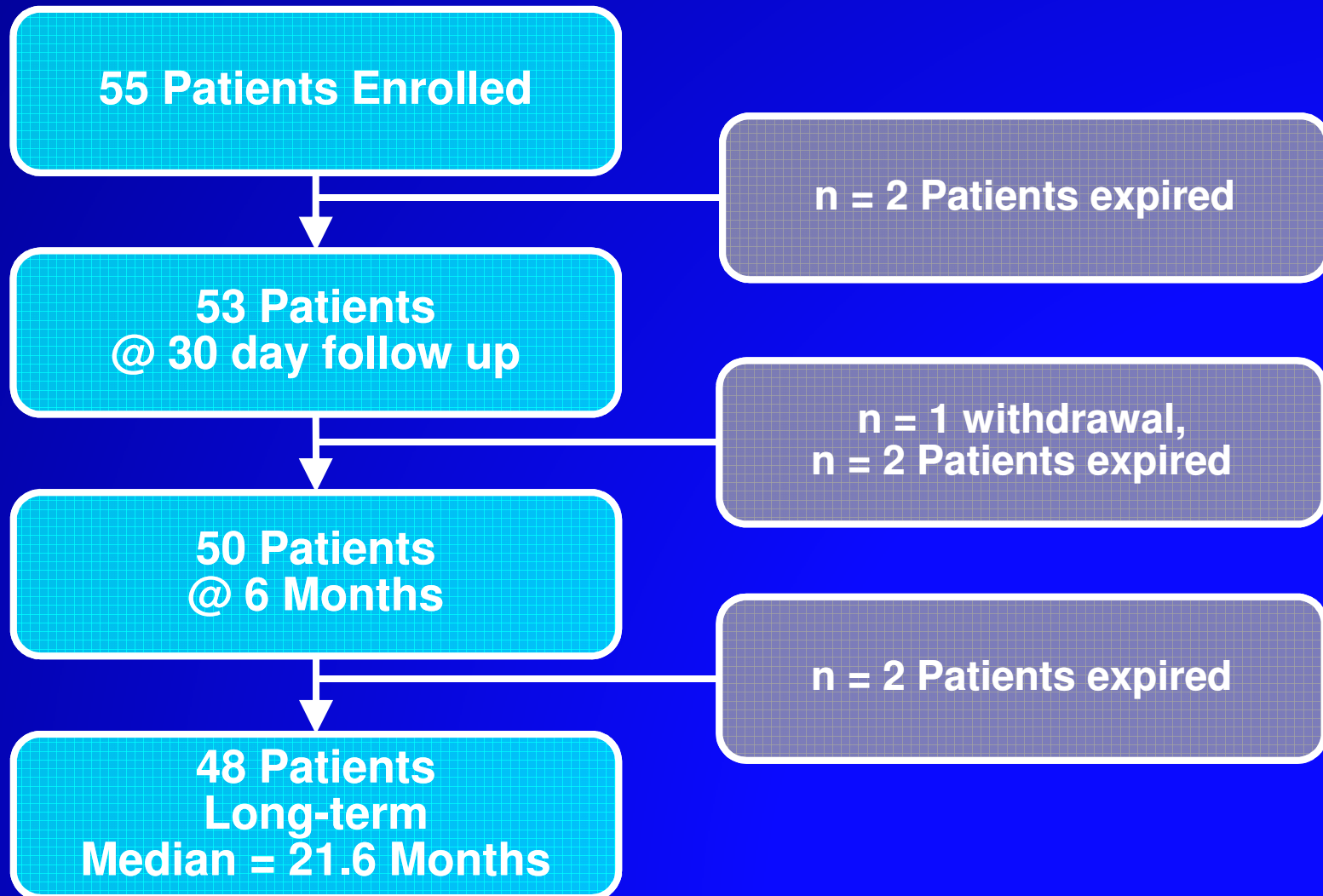
*Conservative estimate since not based on 24-hour Holter

ABLATE Study Results

Interim Analysis (55 Subjects)

- Safety outcomes available for 55 subjects
- Efficacy outcomes available for 29 subjects at 6 months
- Predictive probability of meeting study goal
 - $P_n=0.988$
- Decision: Stop accrual
 - Followed all enrolled patients
 - Perform final analysis

Enrolled ABLATE Patient Disposition



ABLATE Demographics (1 of 2)

ABLATE (N=55)

Age (years)

Mean +/-SD

70.5 +/- 9.3

Median (Min, Max)

72.0 (45.0, 88.0)

%

n

Gender

Male

58.2

32

Ethnic Group

Caucasian

90.9

50

Black

3.6

2

Asian

1.8

1

Hispanic

3.6

2

Pre-existing Pacemaker

12.7

7

ABLATE Demographics (2 of 2)

ABLATE (N=55)

EF (%)

Mean +/- SD

50.0 +/- 10.3

Median (Min, Max)

50.0 (20.0, 70.0)

NYHA Classification

%

n

I

16.4

9

II

41.8

23

III

40.0

22

IV

1.8

1

>80% {

LA Size (cm)

Mean +/- SD

5.9 +/- 1.0

Median (Min, Max)

6.0 (3.9, 7.7)

ABLATE Baseline AF Status

	ABLATE (N=55)	
	%	n
Permanent AF	100.0	55
Longstanding persistent	52.7	29
Persistent	40.0	22
Paroxysmal	7.3	4*

Duration (months) of AF prior to enrollment

Mean +/-SD	61.2 +/- 49.5
Median (Min, Max)	48.6 (1.78, 188.39)

*Paroxysmal Subjects: LA Size > 5 cm: (3/4); Hx of AF > 12 mos (4/4)

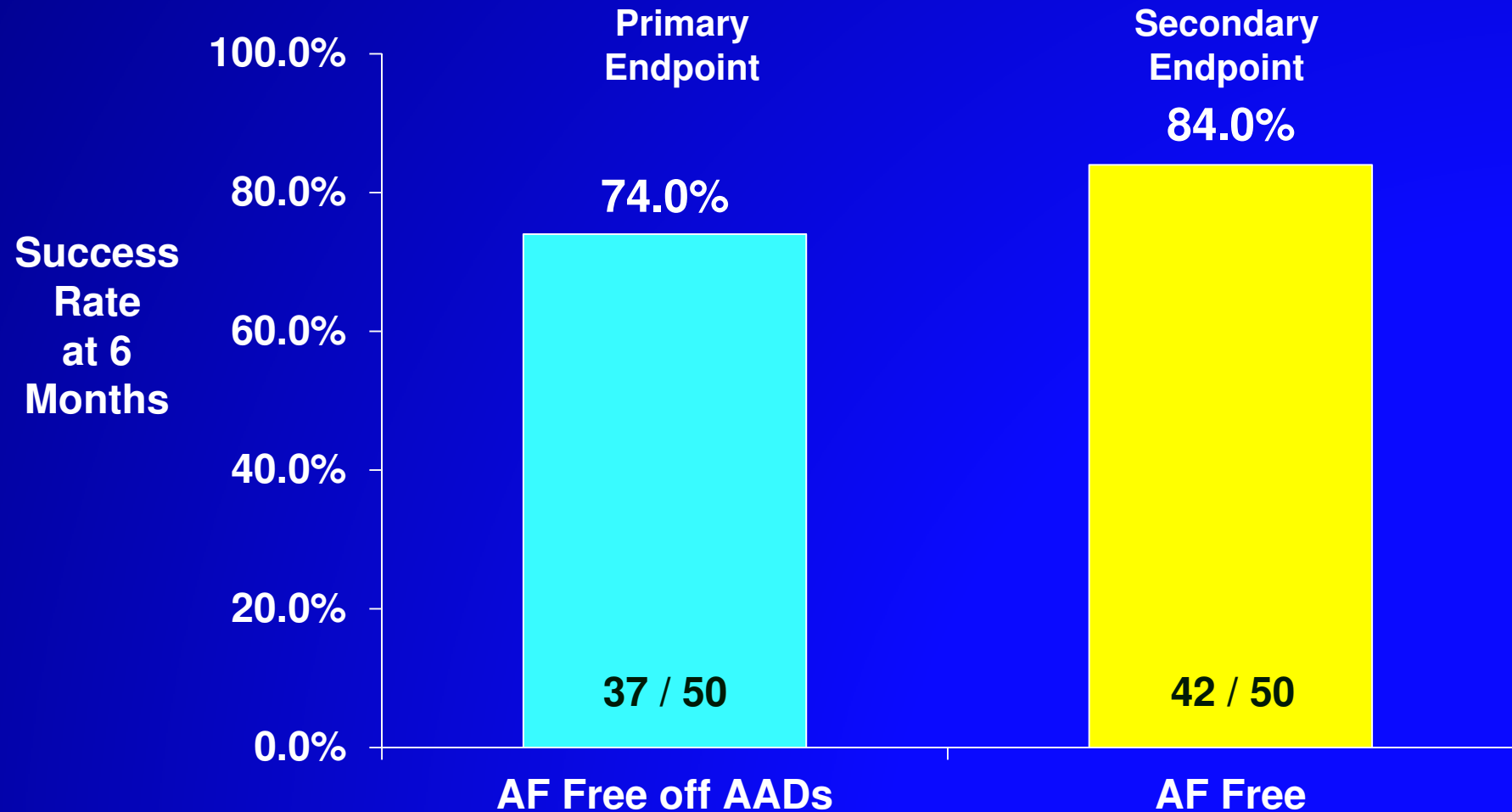
ABLATE Primary Surgical Procedure

Surgery	ABLATE (N=55)	
	%	n
CABG	18.2	10
Mitral Valve	18.2	10
Aortic Valve	21.8	12
CABG & Valve	16.4	9
Double Valve	16.4	9
CABG & Double Valve	9.1	5

ABLATE Primary Safety Endpoint: Primary Safety Endpoint Achieved

Endpoint	%	n
Primary Safety Endpoint	9.1	5
Death within 30 days	3.6	2
Stroke	1.8	1
TIA	0.0	0
MI	0.0	0
Excessive Bleeding (>2 units with reop)	3.6	2

ABLATE Primary Efficacy Endpoint: Primary Efficacy Endpoint Achieved



Primary Endpoint Study Success Goals Achieved

	%	One-sided 97.5% Bayesian CI	Posterior Probability > 60%	Study Goal Met?
PRIMARY EFFICACY				
Free of AF and off AADs at 6 months	74.0	(0.604, 1.00)	97.8%	YES

	%	One-sided 95% Bayesian CI	Posterior Probability < 18.95%	Study Goal Met?
PRIMARY SAFETY				
MAEs at 30 days	9.1	(0.00, 0.179)	96.7%	YES

**Protocol Performance Goals for
Both Safety and Efficacy were
Achieved**

Exploratory Analyses Performed to Answer FDA Questions and Discussion Topics

Caution: analyses are outside the scope of the protocol.
No comparator information available.

FDA Commentary – (Page 25)

As discussed above, the Sponsor is targeting a population of patients with non-paroxysmal AF. Evaluating only non-paroxysmal AF patients reduces the already-small ABLATE data set by 4. Not only does this have possible implications for interpretation of data in the final analyses, but also for the course of study progress. As demonstrated in this section on Interim Analysis, had the Sponsor considered only nonparoxysmal subjects at the time of the Interim Analysis, enrollment would have continued, perhaps yielding a larger analysis cohort.

ABLATE AF Registry

- Enrolling persistent and Longstanding persistent AF subjects
 - Available for FDA submission n=13
 - Currently enrolled n=35 subjects
- Same AtriCure ablation device
- Consistent endpoints and follow-up
- 18 investigational site (3 sites from ABLATE)

Primary Endpoint Hypothesis Testing: Non-paroxysmal Population (ABLATE + ABLATE AF)

	%	One-sided 97.5% Bayesian CI	Posterior Probability > 60%	Study Goal Met?
PRIMARY EFFICACY 43/57				
Free of AF and off AADs at 6 months	75.4	(0.628, 1.00)	99.2%	YES
	%	One-sided 95% Bayesian CI	Posterior Probability < 18.95%	Study Goal Met?
PRIMARY SAFETY 5/64				
MAEs at 30 days	7.8	(0.00, 0.155)	99.0%	YES

FDA Commentary – (Page 35)

Although not formally studied in controlled trials, recent meta-analyses of the literature on surgical ablation for AF reveal the pacemaker implantation rate after treatment to be between 0% and 21%, with a weighted mean of 4.9% for alternative energy sources and 5.8% for the Cox Maze III “cut & sew” technique. There was no significant difference between the two methods. Although not formally tested, the observed rate of pacemaker implantation in ABLATE subjects is higher than the highest rate cited in these reviews for unclear reasons.

- Based on a systematic review of data collected prior to 2005
- Includes subjects with all categories of AF

Current Pacemaker Considerations and the Maze IV Procedure

- Higher after AF surgery¹
- Sinus node overdriven by AF requires PPM implantation
- AADs post op
- Duration of AF
- Type of primary surgical procedure
- Severity of cardiovascular disease

FDA Commentary – (Page 36)

Although not a primary endpoint, FDA believes that device- and AF procedure-related adverse events are important information to track. As such, as noted below, FDA recommends that the safety endpoint of any post-approval study be built around these types of events rather than the MAEs specified above, which are largely due to the concomitant procedure.

Device- and Procedure-related Event Summary

Event	ABLATE (N=51)		ABLATE AF (N=13)		Combined (N=64)	
	n	%	n	%	n	%
Device-related Serious AE	0	0	0	0	0	0
Serious Procedure- related or Indirect Harm	8	15.7	0	0	8	12.5
Non-serious Procedure-related	1	2.0	0	0	1	1.6
TOTAL					9	14.1

Serious Device- and Procedure-related Event Details

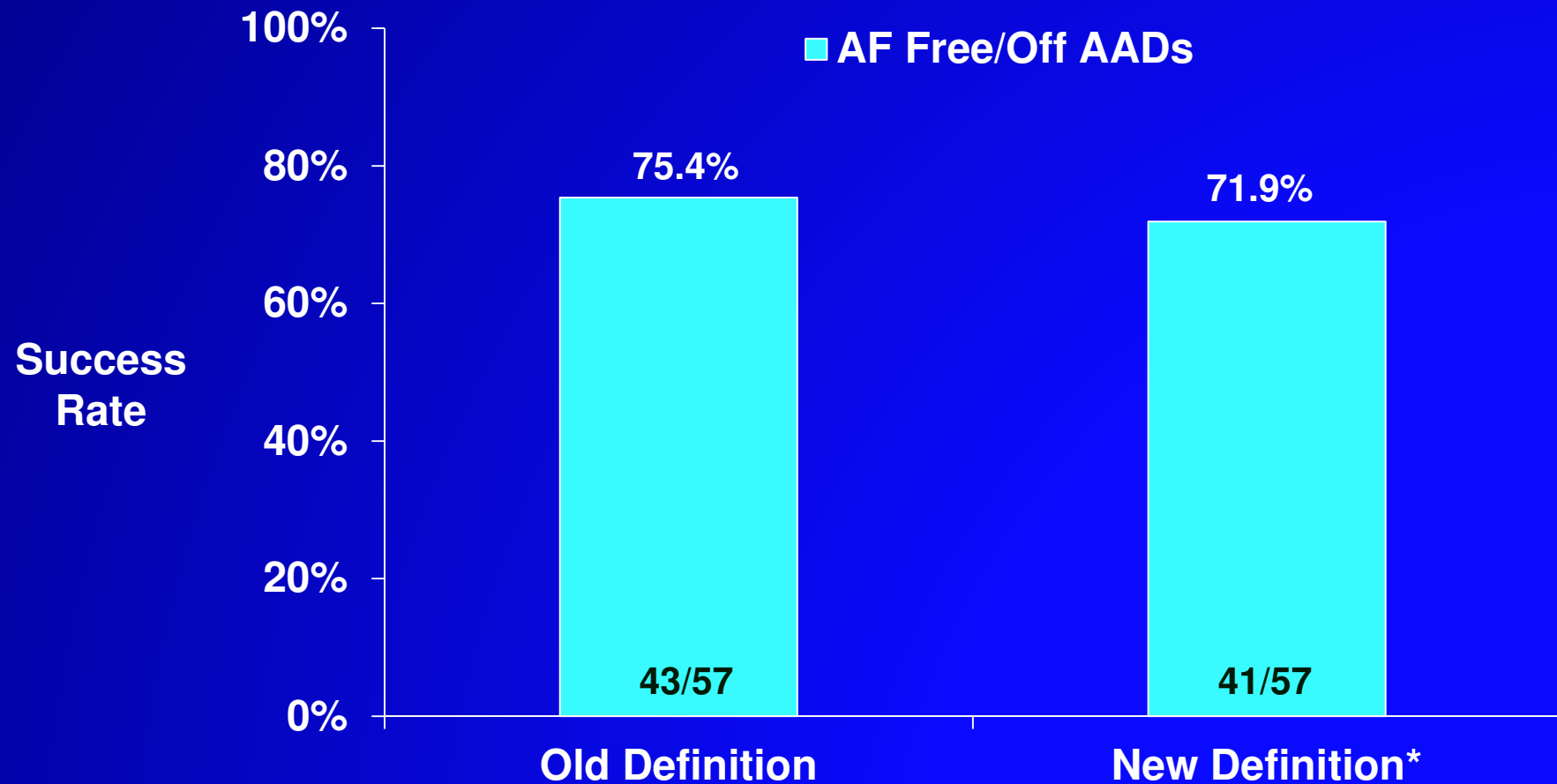
Adjudication	Primary Procedure	Treatment	Primary Safety Endpoint
A-V Node Dysfunction	CABG, MV/TV Repair	Permanent Pacemaker	No
	CABG, MV Replace	Permanent Pacemaker	No
	CABG x3	Permanent Pacemaker	No
	CABG, AVR, MV Repair	Permanent Pacemaker	No
Pulmonary Vein Tear	CABG	Suture	No
Torn IVC at Cannulation Site	CABG x3, AVR	Patch	No
Left Atrial Tear	CABG x2, MV Repair, AVR	Suture	Death
Cardiac Akinesis/ Ischemia	MV/TV Repair	CAB x2	No

FDA Commentary – (Page 16)

As the definition of freedom from AF has changed with the adoption of the 2007 HRS Statement, the Sponsor was asked to provide post hoc analyses defining “freedom of AF” as freedom from episodes of AF, atrial tachycardia, and atrial flutter greater than 30 seconds.

- The revised HRS Consensus Document definition as outlined by FDA, which identifies AF Free as including any episode of AF, Atach or Aflutter lasting 30 seconds or less

Efficacy Outcome Based on Current HRS Consensus: Non-paroxysmal Population



*New Definition AF free defined as no Atrial fibrillation, Atrial flutter, or Atrial tachycardia > 30 seconds

FDA Commentary – (Pages 44/45)

As the sample size of the ABLATE pivotal study is small, although the occurrence of failures due to each of the modes described individually is low, when combined, the observed effectiveness is significantly decreased. FDA is seeking panel input regarding the relative significance of each of the factors described, and whether the risk/benefit profile of the device supports approval of the desired indication when all factors and their weight are considered.

- Inadequate Drug Washout at 6 Months
- Cardioversions Performed
- Lesion Set Deviations
- Consideration of Current Clinical Guidelines

Late Efficacy Assessment Due to Washout

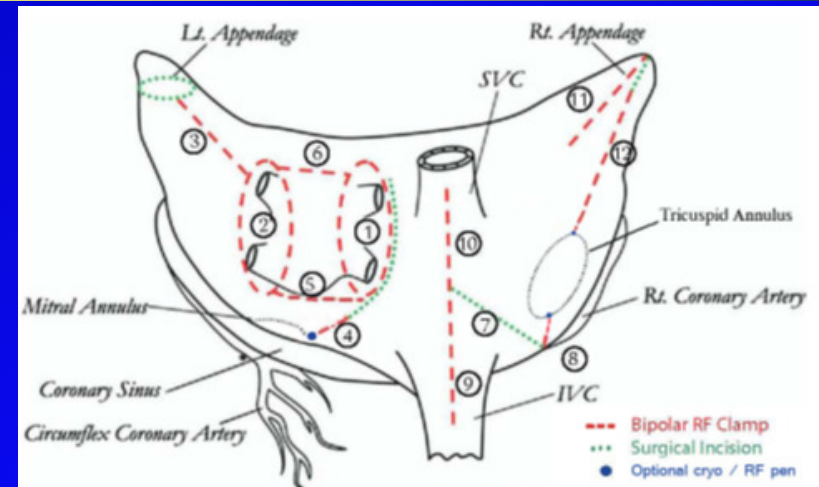
Subjects Affected	Justification	} Deviations, Not Failures
ABLATE: N = 1	<ul style="list-style-type: none">• PI left institution• AF Free on ALL assessments through three years	
ABLATE AF: N = 2	<ul style="list-style-type: none">• Patients 9 days and 22 days out of window	

Cardioversion Between 3 and 6 Months

Subjects Affected	Justification	
ABLATE: N = 1	<ul style="list-style-type: none">• CV day 116 for AF• Numerous assessments negative for AF out to 573	CV allowed per protocol
ABLATE AF: N = 0		

Method for Lesion Creation

- 97% (622/640) of lesions were created per protocol



Subjects Affected

Justification

ABLATE:
N = 8

- Variation per surgeon judgment

ABLATE AF:
N = 2

- Variation per surgeon judgment

Deviations,
Not Failures

HRS Definition of Efficacy

Subjects Affected	Justification	Efficacy presented with this definition and would accept this rate for labeling
ABLATE: N = 2	<ul style="list-style-type: none">• Paroxysmal subject (AF > 30 seconds and < 5 minutes)• Non-paroxysmal subject (Atrial Flutter)	
ABLATE AF: N = 1	<ul style="list-style-type: none">• Non-paroxysmal subject (Atrial Tachycardia)	

Overall Summary

- ABLATE met both primary efficacy and safety endpoints according to the protocol-defined study population
- Data on *non-paroxysmal* patients, including ABLATE and ABLATE AF registry data, supports proposed labeling for persistent and longstanding persistent patients

AtriCure Training Program

David Drachman

President & CEO
AtriCure Inc.

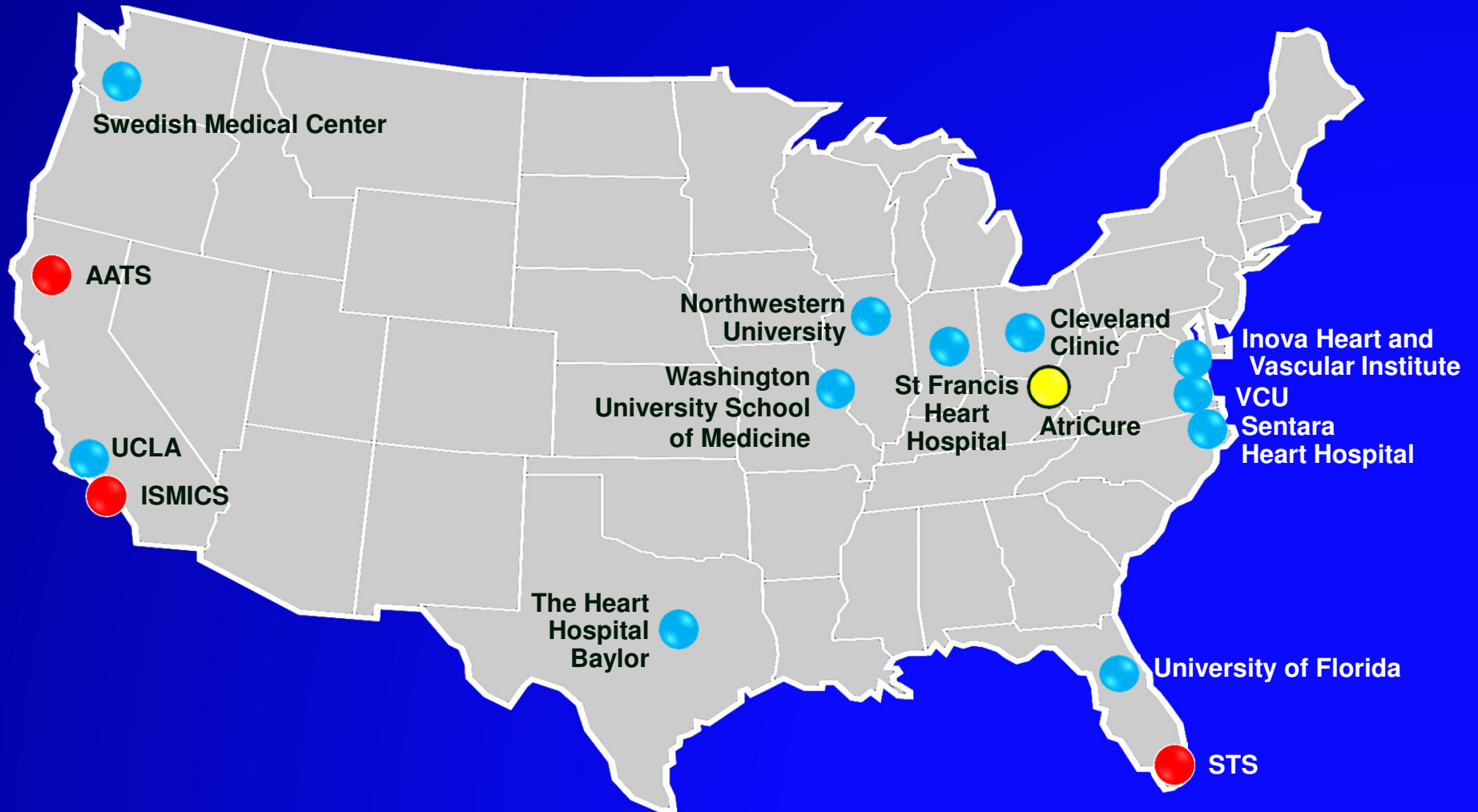
Surgeon Training

- Objectives
 - Train users on the safe and effective use of the Synergy system to perform the Maze IV procedure
 - Provide relevant clinical data and product information
- Timeline
 - Current users of the system will receive training within 18 months of FDA approval
 - New users are trained prior to purchasing the system and require proctoring before receiving their final certification

Education Steering Committee

- Leading cardiac surgeons with expertise in surgical ablation and experienced EP's
- Education Steering Committee Charter
 - Approve surgeon trainers
 - Guide training curriculum
 - Evaluate competency exams and results
 - Monitor program for effectiveness
 - Assess opportunities for improvement

Proposed Training Sites and Events



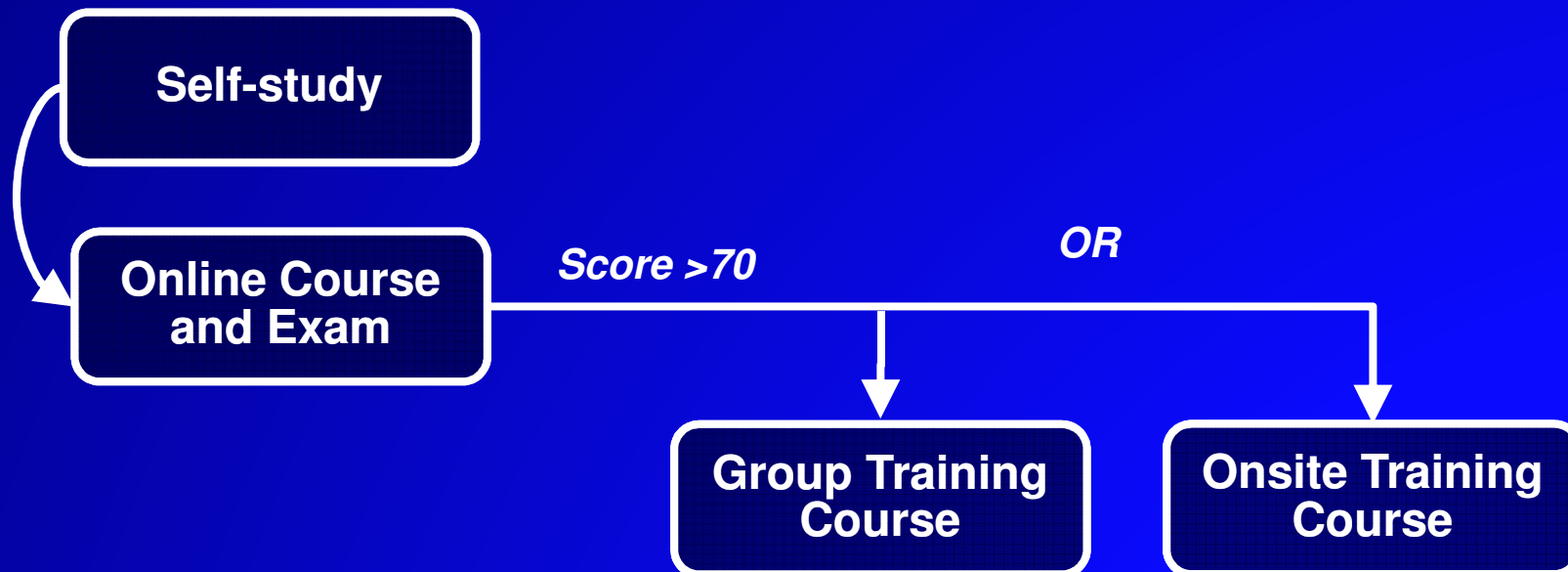
Surgeon Training Progression

- Phase I - Preparatory phase
 - Independent self-paced education
- Phase II - Supervised training
 - Performed by qualified surgeons approved by the Education Steering Committee

Self-study Pre-course and Exam

- AF background, impact to patients
- AF pathophysiology, rationale for lesion set
- AtriCure Synergy Ablation System
- Patient selection and contraindications
- Maze IV concomitant ablation procedure
- Maximizing safety and efficacy
- Post-op and discharge considerations

Proposed Training Program



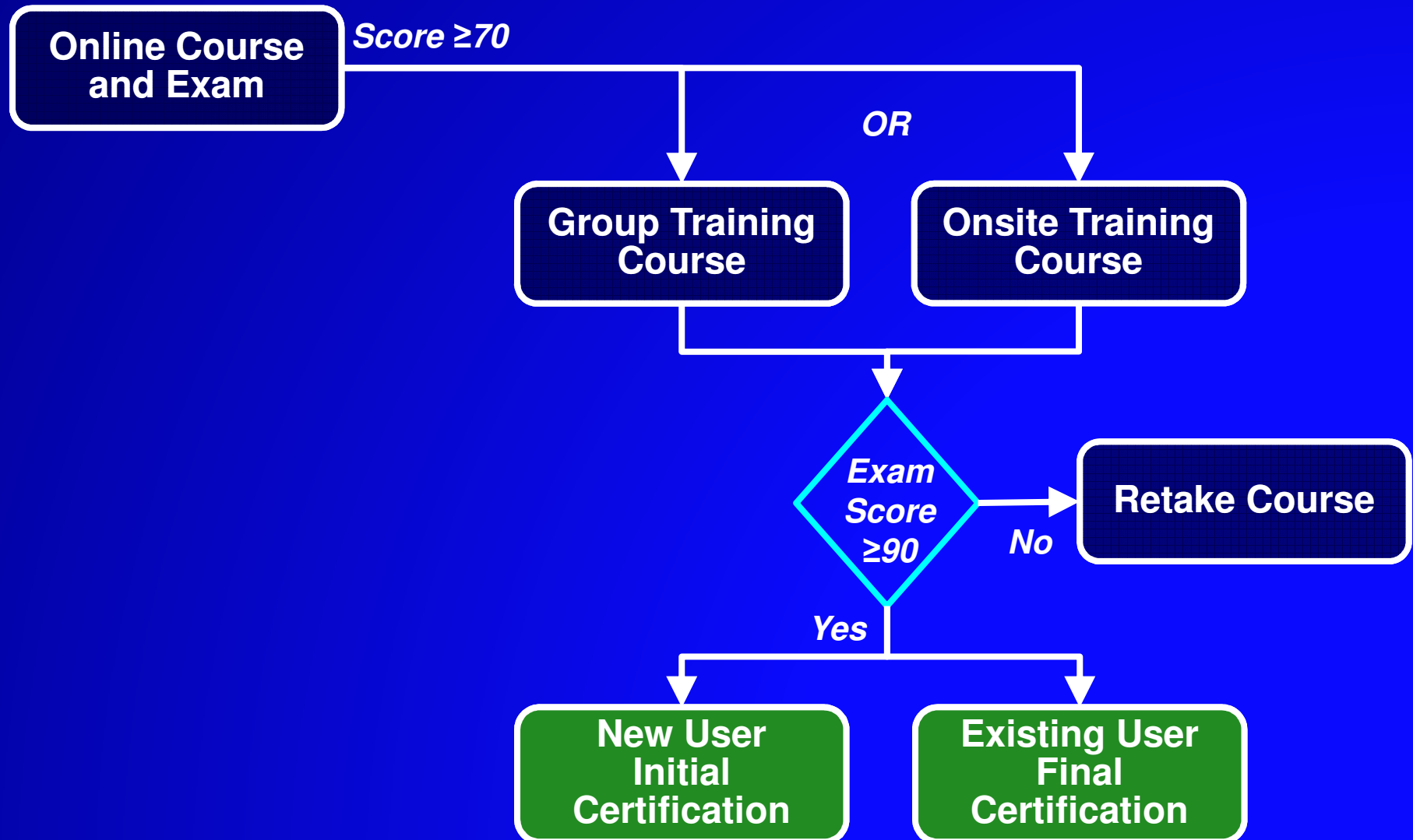
Group and On-site Training Curriculum

- Didactic training curriculum
- Moderated detailed procedure video
 - Optional live case observation
- “Hands On” practicum
 - Replicating the MAZE IV lesion set using a heart/lung block

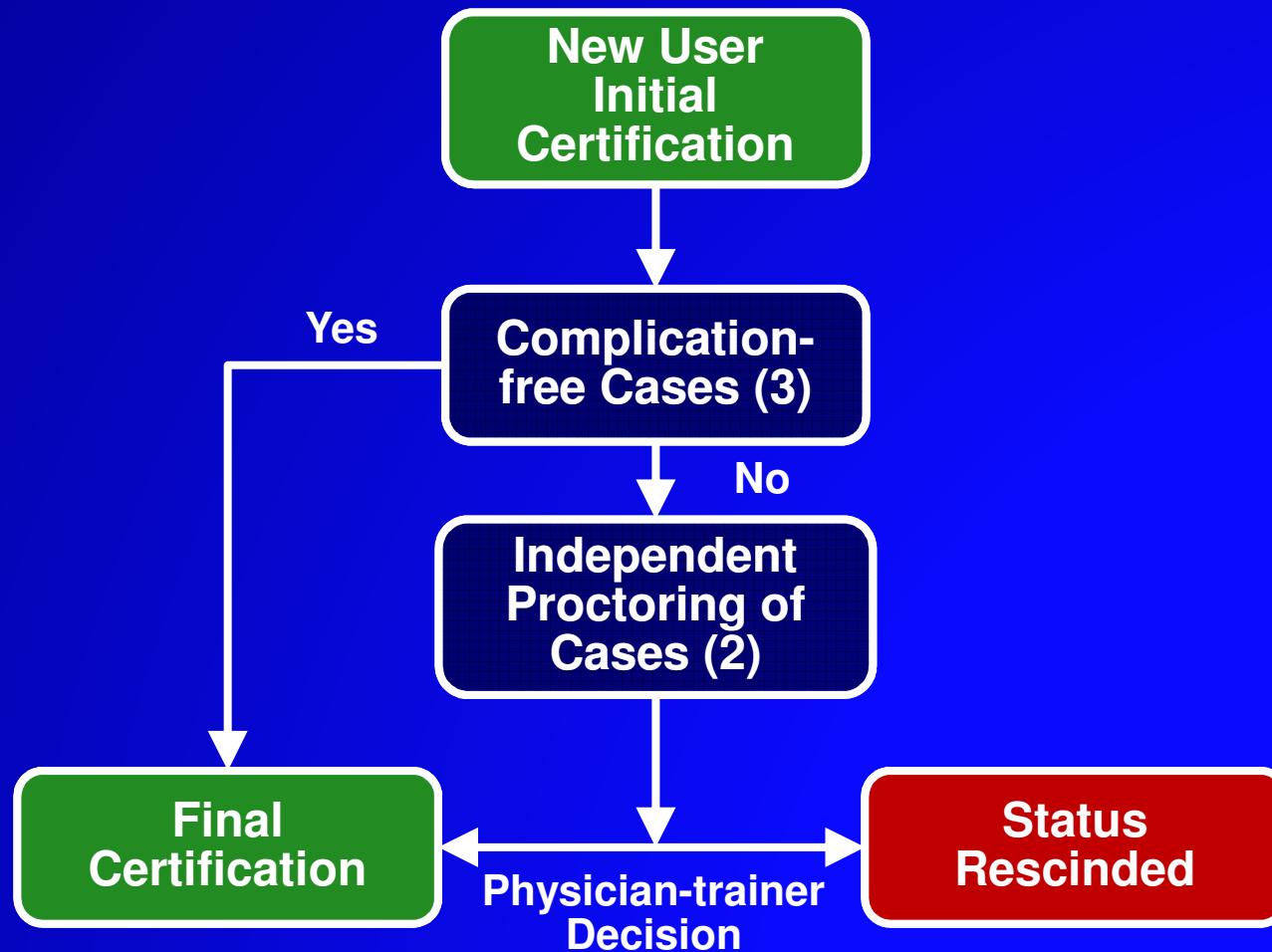
Demonstration of Proficiency in the Practicum

- Setting-up and operating the Synergy system
- Positioning the clamp around the pulmonary veins
- Verifying pulmonary vein conduction block
 - Entrance and exit block
- Using the system to perform linear lesions to complete the Maze IV procedure

Training Program



Additional Requirements for New Users



Training Program Designed to Improve Patient Outcomes

- Comprehensive program
 - Oversight by an Education Steering Committee
- Post Approval Study
 - Monitor effectiveness of training program

Post Approval Study Overview

Lauren S. Baker, PhD

President

Boston Biomedical Associates

Study Design

- Prospective, observational study
- N = 350 subjects
- 50 sites
 - Minimum of 10 new user / sites
- Follow up at 3, 6, 12, 24, 36 months

Primary Efficacy Outcome

- Proportion of patients free from AF
 - Subject off Class I and III AADs and free of AF as determined by 48 hour Holter
 - Assessed at 12, 24 and 36 months

Efficacy Definition

- Freedom from AF
 - 48-hour Holter
 - Absence of AF/AFL/Atach for >30 seconds

Secondary Efficacy Outcome

- Rate of AF Free or AF Free off of AADs at
 - 12, 24, and 36 months

Primary Safety Outcome

- Proportion of patients with any serious device- or ablation procedure–related adverse events occurring post-operatively

Secondary Safety Outcomes

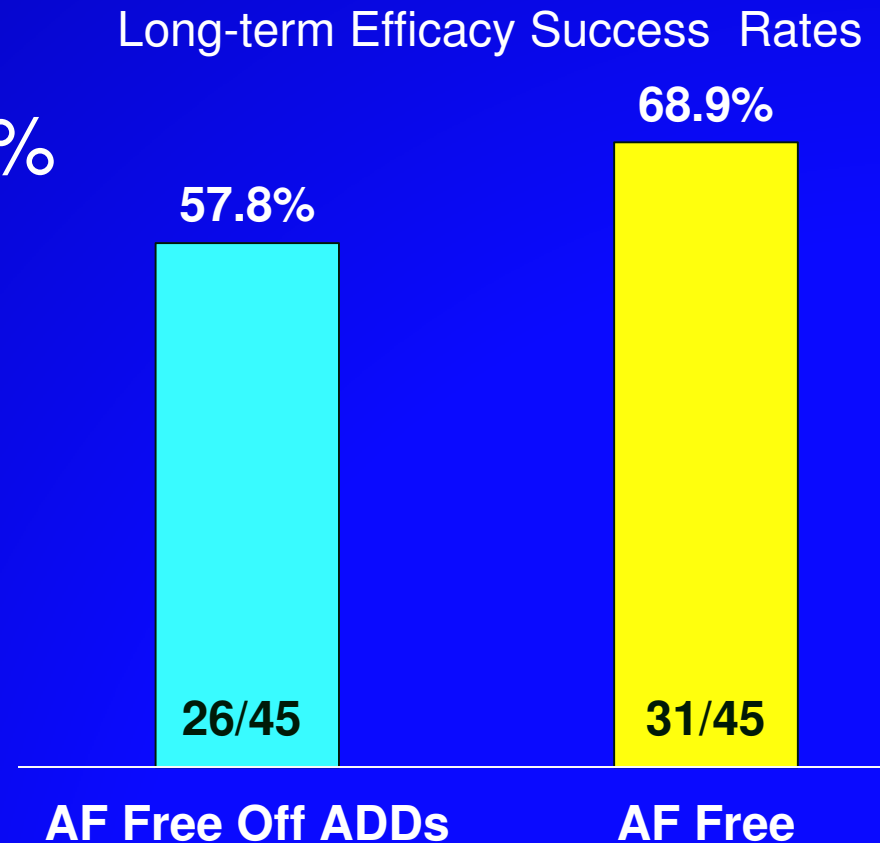
- Incidence of all Adverse Events
 - Serious vs. Non-serious
 - Attribution (device, procedure, other)
- Device/Procedure-related Serious Events
 - Stratified by operation
- Composite Safety Endpoint consistent with ABLATE definition (Death, Stroke/TIA, MI, Bleeding)

PAS Safety Success Criteria

- Target Rate for Primary Safety: 12.5%
- Margin: 5%
- Threshold: 17.5%

PAS Efficacy Success Criteria Based on HRS Definition of AF Free* and Off ADDs

- Target Rate for Primary Efficacy: 57.8%
- Margin: 10%
- Threshold: 47.8%



*New Definition AF free defined as no Atrial fibrillation, Atrial flutter, or Atrial tachycardia > 30 seconds

Feedback on Training Program

- ABLATE to serve as comparator
- Evaluate outcomes and compare to ABLATE
 - Feedback to Education Steering Committee
 - Modifications to training, as appropriate

Post Approval Study Conclusion

- Collection and review of long term efficacy and safety data
- N=350
- Up to 50 centers
- Data to review the effectiveness of training
- Add to the body of surgical ablation of atrial fibrillation

Atrial Fibrillation and Cardiac Surgery

Patrick M McCarthy, MD

Chief of the Division of Cardiac Surgery
Director Bluhm Cardiovascular Institute
Heller-Sacks Professor of Surgery in the
Feinberg School of Medicine



NM Northwestern Memorial[®]
Hospital

Conclusions

- Pre-op AF is a Significant Public Health Problem
- AF Ablation has Disseminated Worldwide
- Safety and Effectiveness has been demonstrated from RCTs; STS; Ablate, and Ablate AF
- Medical Societies Endorse Treatment
- Ultimately, AtriCure is seeking permission to train physicians to properly use the device